Ventilator Associated Pneumonia in a Military Deployed Setting: The Impact of an Aggressive Infection Control Program

Michael L. Landrum, MD and Clinton K. Murray, MD

Background: **Since the onset of military operations in Iraq and Afghanistan, there has been a marked increased in multidrug resistant bacterial infections among combat casualties. We describe the rates of ventilator-associated pneumonia (VAP) before and after the implementation of aggressive infection control measures at the Air Force Theater Hospital in Iraq.**

Methods: **All patients admitted to the intensive care unit (ICU) were followed prospectively for the development of VAP. Baseline VAP rate was determined in May 2006, and preventive measures were implemented by June 2006. Interventions included hand hygiene, contact barrier precautions, patient and staff cohorting, chlorhexidine oral care, and reducing the duration and spectrum of surgical antimicrobial prophylaxis. Additionally, each ICU tent was closed periodically for cleaning and disinfection. Daily inspections provided ongoing staff education and enforcement of procedures. Monthly VAP rates were calculated and compared for trend.**

Results: **There were 475 ICU admissions from May 2006 through August 2006 for a mean admission rate of 119 per month. The rate of VAP per 1,000 ventilator days was 60.6 in May, 31.6 in June, 21.3 in July, and 11.1 in August ($p = 0.029$). Targeted surveillance in November and December revealed VAP rates of 11.6 and 9.7, respectively. Notably, the most common bacteria, *Acinetobacter*, had improved antimicrobial susceptibilities after the interventions.**

Conclusions: **Implementation of aggressive infection control procedures in a combat military hospital was associated with a significant decrease in the rate of VAP. Despite the numerous challenges in theater, infection control can have measurable and sustainable impact in a combat theater hospital.**

Key Words: **Ventilator, Pneumonia, Infection control, Iraq.**

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The military operations in Iraq and Afghanistan are remarkable for an increase in the number of multidrug resistant (MDR) bacteria infecting combat casualties, particularly *Acinetobacter calcoaceticus-baumannii* complex (ABC).[1] Within Iraq, combat support hospitals (CSH) are centralized US military referral healthcare facilities that provide tertiary medical and surgical care to US and non-US personnel. Previous reports have highlighted the frequency with which ABC and other MDR gram-negative bacteria are seen within these hospitals in Iraq,[2] but the sources remain to be definitively described.

Recent publications along with other circumstantial data, implicate nosocomial transmission as the major contributing source of these infections.[3–5] Scott et al. described cluster outbreak strains of ABC within the military healthcare system by pulsed field gel electrophoresis, suggesting that at least in the case of ABC, the bacteria has spread from field hospitals in Iraq to those within the continental US, even to patients with no link to Operation Iraqi Freedom.[5] Other investigations have shown that whereas ABC may colonize the skin of both Iraqi and US troops, MDR strains of ABC responsible for nosocomial infections have not been found on the skin of patients before entering medical care.[3–5] Additionally, ABC strains identical to those found in clinical isolates have been cultured from numerous environmental surfaces from CSH within Iraq.[5] However, it remains unclear whether such environmental contamination contributes to patient transmission.

In nonmilitary US hospitals, ABC is also emerging as an important pathogen, which is difficult to both treat and control.[6–8] Unlike many other gram-negative bacteria, ABC has the ability to survive for extended periods of time on environmental surfaces.[9] One recently described outbreak was attributed to contaminated pulsatile lavage equipment.[6] Although not able to definitively establish causality, the outbreak was controlled after decontamination of potential environmental sources, although other modes of transmission may have contributed.

Efforts to control the nosocomial transmission of these pathogens have been described but no assessment of their efficacy has been reported.[5,6] With nosocomial transmission as the likely source of the ABC outbreak in the US military,

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From the Infectious Disease Service (M.L.L., C.K.M.), San Antonio Military Medical Center, Fort Sam Houston, Texas; and Infectious Disease Clinical Research Program (M.L.L.), Bethesda, Maryland.

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Address for reprints: Clinton K. Murray, MAJ, MC, USA, Infectious Disease Service (MCHE-MDI), San Antonio Military Medical Center, Brooke Army Medical Center, 3851 Roger Brooke Drive, Fort Sam Houston, TX 78234; email: Clinton.Murray@amedd.army.mil.

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effective infection control measures which can be used at CSH are needed urgently. In this report, we describe the aggressive interventions implemented to reduce the nosocomial transmission of ABC and other MDR gram-negative bacteria at a CSH within Iraq, and the associated changes seen in the development of ventilator-associated pneumonias (VAP).

METHODS

Setting

The Air Force Theater Hospital in Iraq serves as one of the Operation Iraqi Freedom CSH providing surgical and medical care to US and non-US personnel. The facility was initially set up in 2003 and, at the time of the interventions described, was composed of interconnected tents set upon a concrete slab floor. Inpatient intensive care unit (ICU) treatment predominantly involves head and neck trauma, severe extremity trauma, and penetrating injuries to the chest or abdomen.

Starting in May 2006 all patients admitted to the ICU were followed prospectively for the occurrence of VAP which was defined according to Centers for Disease Control (CDC) guidelines.[10] Given limitations in microbiologic methods and diagnostic procedures available, patients were classified and treated for VAP if after ≥48 hours of mechanical ventilation they developed fever, leukocytosis, new or progressive pulmonary infiltrate, and purulent tracheobronchial secretions. All classification and treatment decisions were analyzed by a single observer (M.L.L.) on a daily basis. Empiric therapy was chosen based upon knowledge of the most common respiratory isolates and the hospital's antibiogram, and consisted of combination therapy with meropenem 1 g every 8 hours and amikacin 15 mg/kg to 20 mg/kg once daily for patients with normal renal function. Therapy was then tailored after respiratory culture and antimicrobial susceptibility testing on a patient by patient basis. Data regarding short-term (≤7 days) crude mortality was captured, but long-term mortality was not captured because of patient transport to subsequent treatment facilities. This work was conducted as an infection control quality of care activity other than research.

Infection Control Interventions

Interventions began on June 1, 2006 and included the following: placement of alcohol-based hand sanitizer at the bedside of each patient with mandatory hand washing before and after all patient contact; contact barrier precautions with gloves and gown for all patients infected with epidemiologically significant pathogens, specifically *Acinetobacter* spp., extended spectrum beta-lactamase-producing *Klebsiella* spp. and *Escherichia coli*, vancomycin-resistant *Enterococcus* spp., and methicillin-resistant *Staphylococcus aureus*; patient and staff cohorting whenever possible; elevating the head of the bed to at least 30 degrees unless medically contraindicated; chlorhexidine oral care every 6 hours; stopping sedative medications once daily; minimizing use of proton pump inhibitors and H_2-antagonists; and reducing the duration and spectrum of surgical antibiotic prophylaxis. Besides disinfecting all patient care equipment after each patient transfer, each ICU tent (3 in total) including all patient care equipment was periodically (typically monthly) closed for 48 hours and thoroughly cleaned and disinfected.

To minimize the variability of implementing these procedures a standardized preprinted form for all ICU admissions was created incorporating these measures. In addition, antibiotic control measures were instituted. Antimicrobial agents and duration of therapy after surgery were in accordance with currently available guidelines.[11,12] Additionally, different endotracheal tube bite blocks were obtained to facilitate oral care and improve drainage and suctioning of oral secretions.

Finally, at the time of implementation, staff education of physicians and nurses was accomplished regarding the reasoning behind and importance of the plan. All staff were re-educated on a regular basis during the hospital commander's daily morning briefing with hospital personnel. In addition, an infectious disease physician (M.L.L.) inspected the facility multiple times daily with aggressive education and enforcement of procedures.

Statistical Analysis

For the before-after analyses, data were divided into two time periods: baseline period, before initiation of the infection control plan on June 1, 2006, and intervention period, from June 1, 2006 to August 31, 2006. For comparison of antimicrobial susceptibility, data were available for the baseline period from September 2004 to May 2006. For VAP specific comparisons, data were available for a baseline period of May 1, 2006 to May 31, 2006. Categorical comparisons between periods were compared with Mantel-Haenszel χ^2. The incidence rate of VAP was calculated for each month and compared for trend by χ^2. Data analyses were performed using Epi Info, version 5.01 (CDC, Atlanta, GA).

RESULTS

From May 2006 to August 2006 a total of 475 patients were admitted to the ICU for a mean (±SD) of 119 (±20.3) admissions per month. Twenty-five patients were diagnosed with VAP during the same period with the following primary traumatic injury patterns: penetrating injury to the chest or abdomen, 9 (36%); penetrating injury to the head or neck, 9 (36%); extremity trauma, 3 (12%); and multiple sites, 4 (16%). All VAP cases were adult males except for one female adult patient. All patients were intubated orally, and none had any significant comorbid medical conditions known at the time of admission. Median days of mechanical ventilation before onset of VAP was 5 (range, 2–11 days). Sixteen patients had monomicrobial infections (64%), 7 had polymicrobial infections (28%), and 2 patients were culture negative (8%). A total of seven patients died giving a short-term crude mortality of 28% (95% CI: 13%–48%).

Before the implementation of the infection control plan, *Acinetobacter* spp. were the most common clinically significant isolates at the Air Force Theater Hospital accounting for

Table 1 **Antimicrobial Susceptibilities of the Most Common Organisms Isolated at the Air Force Theater Hospital During the Baseline Period From September 2004 to May 2006**

Organism	No. Isolates	Amikacin*	Meropenem*	Ciprofloxacin*	Cefepime*	Oxacillin*	Clindamycin*	Vancomycin*
Acinetobacter spp.	159	41	46	6	12	—	—	—
S. aureus	119	—	—	71	44	44	89	100
E. coli	93	90	100	60	51	—	—	—
K. pneumoniae	66	89	95	68	27	—	—	—
P. aeruginosa	43	95	49	70	27	—	—	—

*Numbers represent percent susceptible.

159 of 580 isolates from September 2004 to May 2006 (27%) (Table 1). The most common respiratory isolates (n = 89) were *Acinetobacter* spp. (55%), *Klebsiella pneumoniae* (15%), *Pseudomonas aeruginosa* (12%), other gram-negative bacilli (15%), and *S. aureus* (3%). From the 14 patients with VAP during May 2006 *Acinetobacter* spp. accounted for 7 of 17 isolates (41%). After implementation of infection control measures on June 1, 2006 *Acinetobacter* spp. remained the most common respiratory isolate in patients with VAP, accounting for 7 of 12 isolates (58%) from 11 patients (p = 0.37 compared with May 2006).

Antimicrobial susceptibilities for all clinically significant isolates of *Acinetobacter* spp. improved after initiation of the infection control plan. For all baseline period *Acinetobacter* spp. isolates the antimicrobial agents with the greatest activity were meropenem and amikacin, with susceptibilities of 46% (73 of 159 isolates) and 41% (65 of 159 isolates), respectively. Susceptibility to meropenem and amikacin increased to 64% (16 of 25 isolates, p = 0.09) and 68% (17 of 25 isolates, p = 0.01), respectively, for the intervention period compared with the baseline period. Specifically, for *Acinetobacter* spp. VAP isolates, for the baseline period from May 1 to 31, 2006, two of seven (29%) were susceptible to meropenem and three of seven (43%) to amikacin. For the intervention period, five of seven (71%, p = 0.12) isolates were susceptible to meropenem and six of seven (86%, p = 0.11) to amikacin.

After introduction of the VAP reduction plan, the rate of VAP steadily decreased through August 2006 (Figure 1). During this same time, days of ventilator use were as follows: May 231 days; June 158 days; July 188 days; and August 180 days. Total VAP rates per 1,000 ventilator days were 60.6 in May, 31.6 in June, 21.3 in July, and 11.1 in August (χ^2 for trend, p = 0.029). Targeted surveillance in November and December revealed sustained improvement in rates of VAP, with rates of 11.6 and 9.7 per month, respectively.

DISCUSSION

Infections have always plagued military campaigns. During the Vietnam War, sepsis was the third leading cause of death among surgical patients treated at combat hospitals within Vietnam.[13] During the current war in Iraq, combat casualties became infected with MDR bacteria. As occurs in most hospitalized settings around the world, nosocomial

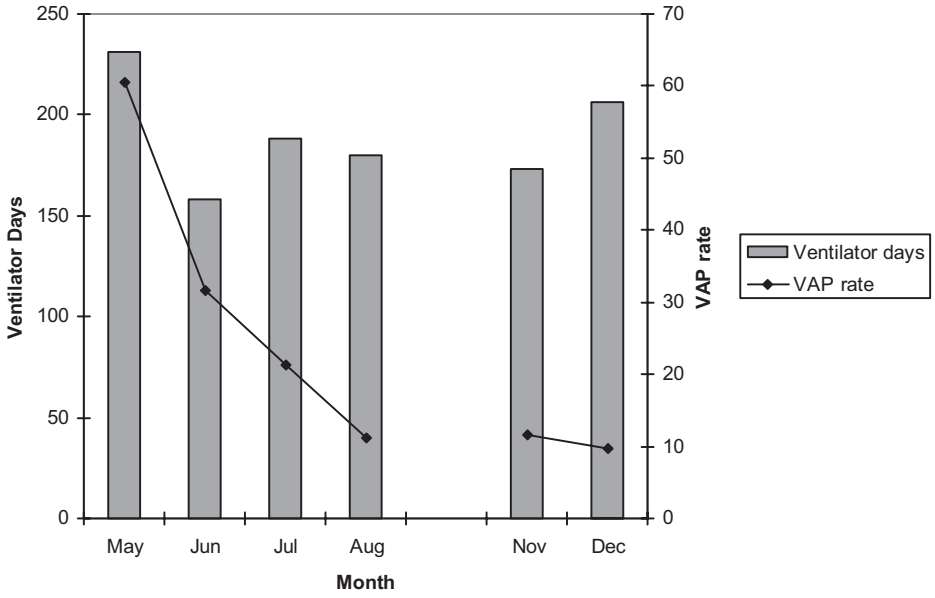

Fig. 1. *Ventilator days and ventilator associated pneumonia (VAP) rate per 1,000 ventilator days from May to December 2006 in the Air Force Theater Hospital, Iraq (χ^2 for trend,* p = *0.029 for May through August).*

transmission plays an important role in propagating these pathogens. We report the exceptionally aggressive and wide-ranging infection control interventions implemented within a combat hospital in Iraq and the associated improvement in antimicrobial susceptibility and reduction in the rate of VAP seen after these interventions. The VAP rates per 1,000 ventilator days decreased from 61 before the interventions to a stable VAP rate of approximately 10. Furthermore, the reduction in VAP rate was sustained after the initial interventions. Based upon these data, it appears that aggressive infection control interventions can be implemented in a combat zone and that these interventions can be effective.

Infection control procedures are increasingly becoming important to help control the global spread of MDR bacteria. The CDC recently released recommendations for controlling MDR infections in the hospital setting.[14] The interventions used to modify the VAP rate in this study include many of the level I (high level of evidence) and level II (moderate level of evidence) recommendations by the American Thoracic Society and the Infectious Disease Society of America for VAP.[10] Our rates were lower than the pooled mean VAP rate of 15.2 for trauma ICUs in the United States per the National Nosocomial Infectious Surveillance System Report.[15] This is truly remarkable when one considers the unique challenges faced in a combat zone. This facility was composed of interconnected tents on cement slabs, had one sink with running water per tent within the facility, there were no isolation rooms, there was limited space between hospital beds which were made of canvas, and the type of injuries treated are associated with the highest rates of VAP in state-of-the-art ICUs. Other described measures to reduce the incidence of VAP, such as subglottic suctioning were not feasible because of limitations of the facility. In addition, there were periods of mass casualties, which overwhelmed the healthcare system and many of the interventions used to prevent nosocomial transmission could not be enforced. There was also a rapid turnover rate of US patients out of the facility after 24 hours to 72 hours whereas non-US patients remained in the facility for extended periods of time. Although this might influence the results of the study, the disposition time for US and non-US patients did not change during the study period. Ultimately this might have a greater impact on nosocomial transmission in other healthcare facilities after US patients leave Iraq.

In addition to the reduction of the rate of VAP, the infection control plan was associated with a significant improvement in the antimicrobial susceptibility of the most common pathogen, *Acinetobacter* spp. One possible explanation for the improved susceptibility is that the antimicrobial selection pressure was reduced with the restriction of antibiotics used for surgical wound prophylaxis as part of the infection control plan. Prolonged surgical antibiotic prophylaxis has been shown to be associated with an increased risk of resistant bacterial infections.[16,17] In one report, receipt of prophylactic antibiotics for >48 hours was associated with a significantly increased risk of pneumonia, particularly from resistant gram-negative bacteria, as well as other complications including *Clostridium difficile* colitis.[17]

Whether reducing the duration or spectrum of surgical prophylaxis results in improved antibiotic resistance or risk of VAP is not entirely clear. However, previous investigations have shown that enforced institutional changes in antibiotic use can be associated with improved antimicrobial susceptibility of gram-negative pathogens.[18,19] One other report also showed that changing the empiric antibiotic regimen for patients with VAP was associated with reduced antimicrobial resistance.[20] Unfortunately, data are not available regarding overall antibiotic use or on the susceptibilities of other respiratory MDR bacteria from our hospital during the study period. Additionally, the improvement in drug resistance seen for all clinical *Acinetobacter* spp. isolates was not definitively seen among VAP isolates because of a smaller sample size. Therefore, future investigations are needed to better understand the relationship between antimicrobial surgical prophylaxis and drug resistant infections, including VAP, in the combat setting.

Although it is remarkable that these rates were achieved and maintained during the study, it is questionable if these interventions are possible within all combat hospitals and during all stages of conflict. During the initial stages of conflict, there is typically rapid movement of medical elements on the battlefield not allowing some of these interventions to be in place. As combat troops transition from rapid movement to stability operations, combat hospitals should adapt appropriate infection control methods in their facility. This will help meet the ultimate goal of minimizing the risk of nosocomial transmission and possibly mitigate the propagation of MDR bacteria throughout the evacuation chain.[5]

Our findings are applicable to nonmilitary healthcare facilities in other austere environments and also to tertiary care referral facilities. As Scott et al. showed, *Acinetobacter* was found on equipment in the CSH and other studies have shown that ABC can survive on environmental surfaces for extended periods of time and these sources often appear to be responsible for the outbreak.[6,7,9] Interventions invoked in this study are relatively simple and included a dedicated focus by the leadership with environmental cleaning, adherence to standard infection control practices such as hand washing, and antibiotic control programs. These measures are possible in all healthcare settings.

We were able to show that the rate of VAP drastically improved after implementation of aggressive and broad reaching infection control measures. In addition, these interventions were associated with a significant increase in antimicrobial susceptibility of the most frequent bacteria seen clinically, with possible implications for future antibiotic control programs. Although it is unclear if this will have an impact upon MDR infections among combat casualties managed in the United States, it is proof that these measures can be used in theater and can be effective.

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DISCUSSION

Dr. Kevin K. Chung (US Army Institute of Surgical Research, Fort Sam Houston, TX): I would like to start by thanking Dr. Murray and Dr. Landrum for their significant contributions, past and present, in the advancement of combat casualty care in the field of infectious diseases. I have no doubt that your tireless efforts have led, and will continue to lead, to improved outcomes for our combat wounded. I am delighted to review their most current contribution as it relates to the impact of aggressive infection control measures that were instituted at the Air Force Theater Hospital in Iraq.

In their report, Drs. Murray and Landrum reveal the results of instituting aggressive infection control measures, to include hand hygiene, barrier precautions, patient and staff cohorting, oral care and selective antibiotic use, on the rate of ventilator-associated pneumonia during a 4-month period with a follow-up surveillance audit a few months later. I was alarmed to read that the incidence of VAP (reported in VAP per 1,000 ventilator days) at this Theater Hospital was 60.6 in May of 06! Compared with the National Nosocomial Infectious Surveillance (NNIS) standards for US trauma ICU (pooled mean VAP rate of 15.2) this incidence is truly striking and disturbing. Clearly a significant problem was identified and something needed to be done. It appears that the Infectious Disease specialist deployed in that hospital that time period (Dr. Landrum) along with his team made this important observation and intervened in a timely fashion. The results are striking. During the span of 4 months, the incidence of VAP plummeted. Down to 31.6 in June, 21.3 in July, and 11.1 (below the national average) in August. These interventions appear to have been "institutionalized" as the follow-up surveillance a few months later, most likely with an entirely new hospital staff, was 11.6 and 9.7 in November and December. In addition, an effect was seen in the antimicrobial susceptibility of our well known multidrug resistant nemesis, acinetobacter. This is a truly significant finding, as it appears that the battle against multidrug resistant acinetobacter can be fought with some success in the "front-line". The less antibiotic pressure applied at the earlier echelons, with resultant improvement in the susceptibility patterns, the better success we can have at eradicating and curing clinically significant acinetobacter infections state-side.

I have one question that may assist in strengthening these causal relationships. What is the monthly breakdown of US versus non-US personnel admissions throughout the study

period? The fact that US personnel are rapidly dispositioned out of theater is an inherent flaw. If there was a significant decrease in non-US personnel admission in the later months, this may be the reason for the drop in VAP rates. Along the same lines, a breakdown in VAP to US and non-US personnel may be helpful.

Lastly, given that the rate of VAP was so high before your intervention, I am left to wonder what our VAP rates are at the other echelon III facilities in theater. Is this a problem at the other Combat Hospitals? Are there efforts underway to identify if this is a theater-wide problem?

Dr. Clinton K. Murray (US Army Institute of Surgical Research, Fort Sam Houston, TX): We appreciate the review and comments by Dr. Chung of our article. Regarding his question of the breakdown of admissions of US personnel and non-US personnel, the admissions of month were: May, 68 US personnel, and 25 non-US personnel; June, 77 and 35; July, 95 and 38; and Aug, 87 and 50. Additionally, during the study, no case of VAP was identified in US personnel as all were transferred rapidly to a higher level of care within 48 hours of admission to the Air Force Theater Hospital.

We too were alarmed at the exceedingly high rate of VAP seen before the implementation of the infection control plan. Comparing our findings to other combat hospitals is difficult, however, for two principle reasons. First, the structure of the Air Force Theater Hospital is different from other CSH in theater. Our facility was composed of interconnected open air tents whereas at least one other facility is a hardened, concrete structure with individual patient rooms. Second, our patient population was unique with a higher proportion of neurosurgical and head and neck trauma patients. Because, these patients are associated with the highest rates of VAP in US hospitals, the Air Force Theater Hospital may have the highest rates of VAP in theater. Efforts to reduce the rate of VAP and other nosocomial infections are ongoing in theater, and further investigation of these interventions are planned.